

### REMARKS/ARGUMENTS

The claims are 2 and 4-9. Claim 9 has been amended to better define the invention and the specification has been amended to correct a translation error. Support for the claims may be found, *inter alia*, in the disclosure at page 9, second paragraph, and page 10, third paragraph. Reconsideration is expressly requested.

Claim 9, with dependent claims 2-5 and 7-8, were rejected under 35 U.S.C. 112, second paragraph, as being indefinite in the use of the term "reactive effectors" which according to the Examiner, could have a number of meanings, including linkage to any biological or chemical molecule that effects some action in vivo.

In response, Applicant has amended claim 9 to specify chemical modification by covalent linkage to chemically reactive effectors of oxygen binding and has amended the specification to change the expression "reactive effectors" to --chemically reactive effectors-- in accordance with the original German

description at page 6, third paragraph, line 4, and respectfully traverses the Examiner's rejection for the following reasons.

On page 9, second paragraph, of the disclosure it can be taken that the hemoglobin may be modified by a covalent linkage to the hemoglobin to modify the affinity and cooperativeness of the ligand binding. Because the ligand of hemoglobin is oxygen, it is respectfully submitted that the chemically reactive effectors which can be used for such modification are clearly those affecting the oxygen binding. See also page 10, third paragraph, lines 1-6 of the disclosure where it is pointed out that a modification (of the hemoglobin) can be performed "with chemically reactive effectors such as ...." or also via "chemically unreactive effectors of the oxygen binding [=ligand binding]...."

Moreover, it is respectfully submitted that the terms "chemically reactive" as well as "effectors" are known in the art as can be seen from the following:

I) "Chemically reactive" is a technical term which

implicitly includes the capability of a compound to chemically react with another, see e.g.

<http://en.wikipedia.org/wiki/Reactive>: where it is pointed out "Reactive can refer to:

- Generally, capable of having a reaction...."

Alternatively see also

[http://en.wikipedia.org/wiki/Chemical\\_reaction](http://en.wikipedia.org/wiki/Chemical_reaction):

where it is pointed out:

"A chemical reaction is a process that always results in the interconversion of chemical substances. The substance or substances initially involved in a chemical reaction are called reactants. Chemical reactions are usually characterized by chemical change, and they yield one or more products...." (Footnotes omitted)

The above Wikipedia citations are included in Attachment 1.

II) "Effectors" is disclosed e.g. in:

[http://en.wikipedia.org/wiki/Effector\\_\(biology\)](http://en.wikipedia.org/wiki/Effector_(biology)) where  
it is pointed out:

"An effector is a molecule...that binds to a protein  
and thereby alters the activity of that protein...."

See Attachment 2.

For overall use of the above terms please also see

<http://www.pantherdb.org/panther/category.do?categoryAcc=BP00063>

(Attachment 3 hereto); where the following may be found as  
regards the definition of protein modification:

"The post-translational modification of proteins via creating a  
covalent bond ...."

Other citations that use different terms for defining the  
same subject matter are:

NACHARAJU P. ET AL: "Combining the Influence of Two Low

O<sub>2</sub> Affinity-Inducing Chemical Modifications of the Central Cavity of Hemoglobin", *Biochemistry* 46 (2007): 4554-4564 (Attachment 4);

and

Huang K.-T, Lin Y.-L.: "Modified Hemoglobin with Allosteric Effector Conjugated", U.S. Patent Application Publication No. 2008/0064855 A1, March 13, 2008 (Attachment 5).

It is respectfully submitted that claim 9 as amended is specifically clear in specifying the further chemical modification by at least one of covalent linkage to chemically reactive effectors of oxygen binding, and covalent linkage to other macro molecules selected from the group consisting of poly(ethylene oxides), poly(ethylene glycols), dextrans, and hydroxyethylstarches. Accordingly, it is respectfully submitted that the rejection under 35 U.S.C. 112, second paragraph, should be withdrawn.

Claims 2-9 were rejected under the judicially created doctrine of obviousness-type double patenting as being

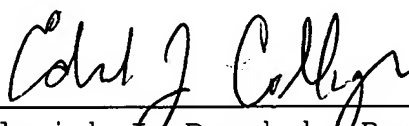
unpatentable over claims 14-16 of *U.S. Patent No. 6,956,025* or claims 15-17 of *U.S. Patent No. 7,005,414*.

In response, without conceding the propriety of the Examiner's rejection and in order to expedite prosecution, Applicant is submitting herewith Terminal Disclaimers with respect to the '025 and '414 patents, thereby obviating the double patenting rejections.

In summary, claim 9 has been amended along with the specification. In addition, Terminal Disclaimers with a check in the amount of \$140.00 in payment of the Terminal Disclaimer fees for a Small Entity for both Terminal Disclaimers is enclosed. In view of the foregoing, withdrawal of the final action and allowance of this application are respectfully requested.

Respectfully submitted,  
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Enclosures:

Terminal Disclaimer of U.S. Patent No. 7,005,414  
Terminal Disclaimer of U.S. Patent No. 6,956,025  
Check in the amount of \$140.00 (\$70.00 each)  
Attachments 1, 2, 3, 4 and 5

I hereby certify that this correspondence is being deposited with the U.S. Postal Service as first class mail in an envelope addressed to: MAIL STOP AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on June 3, 2009.

  
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Amy Klein

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